Continuous Fermentation: Prospects for Future Rollout

BIO Pacific Rim Summit

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Agenda

- A Brief Introduction to Nexant
- A Background in Continuous Fermentation
- Continuous Fermentation Process Types
- What does the future hold?
- Conclusions
A Brief Introduction to Nexant
Nexant Consulting is a global consultancy covering the energy/chemical value chain

Oil and Gas

UPSTREAM
- Resource Evaluation
- Exploration & Drilling
- Oil & Gas Service
  - Sector Planning
  - Shale Gas & Oil
  - Coal
- Processing
- LNG Liquefaction
- LNG Shipping & Regasification
- Oil & Gas Pipelines
  - Gas Processing
  - Gas Distribution
- Petroleum Refining
- Product Market Assessment
  - Coal to Liquids
  - Gas to Liquids

DOWNSTREAM

MIDSTREAM

Chemicals and Clean Tech

CHEMICALS
- Gas & Naphtha Based Petrochemicals
- Olefins & Aromatics
- Polymers
- Intermediates
- Ammonia & Fertilizers
- Specialty Chemicals
- Advanced Materials

GREEN CHEMICALS
- Biofeedstocks
- Syngas
- Biopolymers
- Olefins
- Alcohols
- Aromatics
- Sourced from Biomass, Algae, Wastes, and Agricultural Sources

RENEWABLE ENERGY
- Biomass
- Gasification
- Solar (Thermal & PV)
- Wind Power
- Clean Coal
- CO₂ Capture and Sequestration
- Fuel Cells & Hydrogen
- Geothermal

Nexant has completed over 3,000 client assignments in over 100 countries, and has over 600 employees
Recent special reports indicate Nexant’s commitment to understanding green technology

- Biobutanol and Downstream Markets: Will You be Buying Bio?
- Cellulosic Sugars: Unlocking Biomass’ Potential
- Next Generation Biofeedstocks: Resources for Renewables
- Biobased Chemicals: Going Commercial
- Plants To Plastics
- Bio-Butanediol: Is Bio-Butanediol Here to Stay?
- From Diapers to Paints - Is Bio-Acrylic Acid on the Way?
- Bio Routes to $p$-Xylene
- Plastics from Trees
- Algae Technology
- Bio-Succinic Acid
- Bio-Jet Fuel
- Bio-Naphtha: Missing Link to the Green Chemicals Value Chain

See www.nexantthinking.com for an abstract, prospectus, or order forms
Nexant is developing a comprehensive subscription based multiclient service on the bio sector

- Products will be covered by value chain on a three-year rotating basis with quarterly updates

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<th>C4, Aromatics &amp; Other</th>
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<td>Pyrolysis Oil</td>
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This list is preliminary and comments from potential subscribers are welcome
A Background in Continuous Fermentation
The concept of continuous fermentation

Continuous fermentation does not have to run on a batch cycle and can operate without interruption
There are many other advantages of continuous fermentation processes

- More consistent productivity
- Higher average cell loading
- Gas recovery is much easier
- Steady state operation simplifies operation in other units
- Much greater potential for optimization
- Increased capital utilization and lower capex
- Less physical space required
- Reduced energy consumption (and lower peak loads)
- Labor productivity Increase
- Fewer cleaning intervals
- Consistent product output – an end to batch variation
- Contaminants can wash out (in free cell systems)
Continuous fermentation is the “Holy Grail” of fermentation engineering. Many have hunted for it...
... But few have succeeded. Why?
There are many technical challenges...

- Contamination is more serious than in batch and septic control is difficult
- Washout of producing organism becomes possible
- Long culture age means unexpected behavior can occur, especially for metabolically inferior GMOs
- Higher stability and reliability requirements
- Operation with anything but growth-linked product is very difficult
- Low productivity, titer and desire for optimization often requires multiple fermenters in series
And there are many operational challenges

- Higher operating complexity, which means:
  - Staff need higher skill level
  - More requirements for controls and instrumentation

- Process configuration displays lack of flexibility in:
  - Output – fermentation operates at all or nothing
  - Types of products that can be produced

- Long startup time required in order to reach steady state (sometimes >2 weeks)
Many continuous fermentations have been attempted, but few have gotten off the ground

- Successful commercial implementations are few and far between:
  - Brazilian cane ethanol industry
  - Dominion Brewing (New Zealand) – the Coutts process
  - Anaerobic waste treatment
  - Biogas digesters
  - Immobilized lager maturation and alcohol-free beer production (e.g., Sinebrychoff Brewery of Finland)
  - Lacto-fermentation of milk (yogurt production)
  - “Quorn” mycoprotein and “Pruteen” single-celled protein feed (originally by ICI)

- Meanwhile, failures litter the landscape, many of which have never left the research stage
Continuous Fermentation Processes
Free cell systems are the oldest and dominant commercial type

Free cell systems have a high degree of technical complexity but easily discharges aged cells and has resistance to contamination.
Immobilized cell systems have cells anchored on packing, much attention but few commercial implementations.

Immobilized Cell Fermenter

Immobilization simplifies operation but complicates maintenance and introduces more risks from aged cultures and contamination.
Membrane bioreactors exist only in wastewater treatment, but have great potential in chemicals and fuels.

Selective membranes give potential benefits beyond particulate filtration.
What does the future hold?
Successful examples of continuous fermentation share a common characteristic: Robust organisms

- Focus on relatively robust fermentative organisms
  - e.g., anaerobic mixed cultures (waste treatment), brewer’s yeast (beer), *F. venetatum* (mycoprotein), lactobacilli (yogurt), simplifying operations

- **Activated Sludge**
- **Brewer’s Yeast** (*Saccharomyces cerevisiae*)
- **Fusarium venetatum**
Another common characteristic of continuous fermentations: Products

- In many applications, the whole fermentation broth is the product (beer, yogurt) or the biomass is the product (mycoprotein, single-celled protein), simplifying separation and (sometimes) operation.
Successful continuous fermentations share common drivers for adoption

- Historically, a big push for wholesale adoption of continuous fermentation came from massive competition in the commercial brewing industry in the 1960s to 1970s. Drivers then were:
  - Strong price competition for saturated markets
  - Relatively uniform products
  - An emphasis on marginal production efficiency and efficient capital utilization
  - Perception that the returns to batch fermentation technology were diminishing

- In certain markets, these drivers are once again beginning to come to the forefront

Ultimately, the beer industry responded through product differentiation and new innovations in batch processing, but for biofuels and biochemicals, the same options may not be available
Membrane bioreactors offer the most potential for commercial production of biofuels and biochemicals

- Membrane integrated systems carry most of the advantages of free-cell reactors
- Potential applications include:
  - Separation of microbes
  - Concentration product at titer higher than in fermentation broth
  - Separation of byproducts
  - Separation of fermentation inhibitors
- Although not a direct fermentative application, these systems also can be placed in upstream saccharification systems to deliver “clean” sugars to sensitive organisms and recycle enzymes

The main barrier to implementation of membrane continuous reactors is the development of appropriate membranes for specific products
Multiple technology developers are currently working to commercialize continuous fermentations

- A notable example is LanzaTech, which is pursuing a continuous syngas fermentation for ethanol and 2,3-BDO

LanzaTech 100 kgal/y Demonstration Plant at BaoSteel, in operation for >8 months

Graphics courtesy of LanzaTech
Multiple technology developers are currently working to commercialize continuous fermentations

- A second notable example is Cobalt Technologies, which is working to produce n-butanol from (cellulosic) sugars through a continuous immobilized fermentation.
Conclusions
Rollouts of continuous fermentation: What will they look like?

- Expect to see the strongest pushes for continuous fermentation develop in areas of established, large volume bioproducts where there is strong price competition

  - Robust organisms producing natural primary metabolites are more likely to succeed

  - Feed sterilization will improve continuous fermentation’s value proposition

  - Newly commercializing bioproducts will most likely not move to continuous fermentation unless it is needed to establish a competitive market position
What should we expect to see?

- Expect to see continuous fermentation in commercialized second generation biofuels and biochemicals.
- Expect to see non-traditional, membrane integrated continuous fermentations become more significant, especially where membrane processes are already used.
- Ethanol, butanols, stereospecific lactic acid, and succinic acid are sectors that display the strongest drivers for adoption of continuous fermentation.
Questions?

THANK YOU

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